

## CLAIMS

1. A process for producing a chimaeric viral vector comprising;  
5 culturing a host cell which comprises one or more Simian Immunodeficiency Virus (SIV) nucleic acid sequences capable of producing an SIV capsid and which further comprises a vector comprising a Human Immunodeficiency Virus type 2 (HIV-2) packaging signal and a heterologous nucleic acid sequence;  
10 said vector being packaged in the SIV capsid to produce a chimaeric virus comprising the heterologous nucleic acid sequence.
2. A process according to claim 1 comprising infecting the host cell with the vector which comprises the human Immunodeficiency  
15 Virus type 2 (HIV-2) packaging signal and a heterologous nucleic acid sequence.
3. A process according to claim 1 comprising infecting the host cell with a first vector which comprises the one or more Simian  
20 Immunodeficiency Virus (SIV) nucleic acid sequences capable of producing an SIV capsid and a second vector which comprises the human Immunodeficiency Virus type 2 (HIV-2) packaging signal and a heterologous nucleic acid sequence.
- 25 4. A process for producing a Simian Immunodeficiency Virus (SIV) encoding a heterologous gene, which process comprises infecting a host cell with a first vector which is capable of producing SIV capsid and a second vector comprising a Human Immunodeficiency Virus type 2 (HIV-2) packaging signal sufficient to package the  
30 vector in the SIV capsid and a heterologous gene capable of being expressed by the vector; and culturing the host cell.
5. A process according to claim 3 or 4 wherein the first vector is a SIV vector comprising a mutation within an SIV packaging  
35 signal such that viral RNA is not packaged within an SIV capsid.

6. A process according to claim 5 wherein the first vector is a packaging defective SIV vector
7. A process according to claim 5 or claim 6 wherein said  
5 mutation comprises a deletion in the region between the primer binding site and the 5' major splice donor site of SIV.
8. A process according to claim 9 wherein said mutation  
comprises a deletion within the DIS structure.
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9. A process according to claim 7 or claim 8 wherein said  
mutation comprises a deletion of:  
a sequence of SEQ ID NO: 2;  
a fragment thereof of 5 or more nucleotides in length; or  
15 a variant of either thereof.
10. A process according to claim 9 wherein said mutation  
comprises a deletion in the region of nucleotides 53 to 85 of SEQ  
ID No 2
- 20
11. A process according to any one of claims 5 to 10 wherein said  
mutation comprises a deletion in the region between the 5' major  
splice donor and the *gag* initiation codon
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12. A process according to claim 11 wherein said mutation  
comprises a deletion of:  
a sequence of SEQ ID NO: 3;  
a fragment thereof of 5 or more nucleotides in length; or  
a variant of either thereof.
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13. A process according to any one of claims 3 to 12 wherein the  
first vector does not comprise replication-competent SIV.
14. A process according to any one of the preceding claims  
35 wherein the SIV capsid comprises an envelope protein from a  
retrovirus other than SIV

15. A process according to claim 14 wherein the nucleic acid sequence encoding the envelope protein from a retrovirus other than SIV is operably linked to an 5' LTR sequence from the same retrovirus

16. A process according to any one of claims 3 to 15 wherein said second vector comprises:

- (a) a sequence of SEQ ID no 1 or a variant thereof,
- (b) an internal fragment thereof of 5 or more nucleotides in length, or
- (c) a fragment thereof of 17 or more nucleotides in length.

17. A process according to any one of claims 3 to 16 wherein said second vector comprises the matrix (MA) region of the gag ORF or a fragment thereof.

18. A process according to any one of claims 3 to 17 wherein said second vector comprises nucleic acids 553 to 912 of HIV-2 RNA or a fragment thereof.

19. A process according to any one of claims 3 to 18 wherein the second vector is replication deficient.

20. A process according to one of claims 3 to 19 wherein the second vector comprises one or more nucleic acid sequences from the 5' and 3' LTRs of HIV-2, which direct the expression and reverse transcription of the second vector and the integration of the second vector into the genome of a target cell.

21. A process according to claim 20 wherein the second vector comprises a mutation in the U3 region of the 3' LTR of the vector, said mutation being copied during reverse transcription such that the long terminal repeat promoter is inactivated

22. A process according to any one of claims 3 to 21 wherein the second vector comprises a promoter region operably linked to the heterologous gene or nucleic acid sequence.
- 5 23. A process according to any one of claims 3 to 22 wherein the said first and/or second vector are integrated into the genome of the host cell.
- 10 24. A process according to any one of claims 3 to 22 wherein the said first and/or second vector are extra-chromosomal in the host cell.
- 15 25. A process according to any one of the preceding claims wherein the heterologous gene or nucleic acid sequence encodes a therapeutic protein or peptide, an antigen protein or peptide.
- 20 26. A process according to any one of the preceding claims comprising isolating and/or purifying the virus comprising the heterologous nucleic acid sequence.
- 25 27. A process according to any one of the preceding claims comprising formulating the virus comprising the heterologous nucleic acid sequence with a pharmaceutically acceptable excipient.
28. A process according to any one of the preceding claims wherein the virus is suitable for infection of human and non-human primate cells.
- 30 29. A process for making a producer cell for the generation of chaemic virus comprising:
- 35 infecting a host cell which comprises one or more Simian Immunodeficiency Virus (SIV) nucleic acid sequences capable of producing an SIV capsid, with a vector comprising a Human Immunodeficiency Virus type 2 (HIV-2) packaging signal and a heterologous nucleic acid sequence.

30. A process according to claim 29 wherein the host cell is infected with a first vector which comprises the one or more Simian Immunodeficiency Virus (SIV) nucleic acid sequences capable of producing an SIV capsid

31. A process according to claim 29 or claim 30 comprising isolating and/or purifying the infected cell.

32. A process according to any one of claims 29 to 31 comprising culturing said infected cell.

33. A virus produced by a process of any one of claims 1 to 28.

34. A virus according to claim 33 which is capable of infecting human and non-human primate cells.

35. A host cell infected with a first vector which is capable of producing SIV capsid and a second vector comprising a Human Immunodeficiency Virus type 2 (HIV-2) packaging signal sufficient to package the vector in the SIV capsid and a heterologous gene capable of being expressed by the vector

36. A host cell produced by a process of any one of claims 29 to 32.

37. A host cell according to claim 35 or claim 36 which is a human or non-human primate cell.

38. A vector system comprising a first vector which is capable of producing SIV capsid and a second vector comprising a Human Immunodeficiency Virus type 2 (HIV-2) packaging signal sufficient to package the vector in the SIV capsid and a cloning site suitable for insertion of a heterologous gene capable of being expressed by the vector.

39. A vector system according to claim 38 wherein a heterologous gene is inserted into the cloning site.

40. A kit comprising a first vector which is capable of producing  
5 SIV capsid and a second vector comprising a Human Immunodeficiency  
Virus type 2 (HIV-2) packaging signal sufficient to package the  
vector in the SIV capsid and a cloning site suitable for inserted  
of a heterologous gene capable of being expressed by the vector...

10 41. A method of producing a pharmaceutical composition for use in  
gene therapy comprising;  
producing a virus by a process of any one of claims 1 to 28,  
and;  
formulating the virus with a pharmaceutically acceptable  
15 excipient.

42. A pharmaceutical composition comprising a virus according to  
claim 33 or 34, a vector system according to claim 38 or 39 or a  
host cell according to any one of claims 35 to 37, and a  
20 pharmaceutically acceptable carrier.

43. A virus according to claim 33 or 34, a vector system  
according to claim 38 or 39 or a host cell according to any one of  
claims 35 to 37 for use in gene therapy of a human or non-human  
25 primate.

44. Use of a virus according to claim 33 or 34, a vector system  
according to claim 38 or 39 or a host cell according to any one of  
claims 35 to 37 in the manufacture of a medicament for use in gene  
30 therapy.

45. Use according to claim 44 wherein the medicament is for use in  
a human or non-human primate.

35 46. Use according to claim 44 or 45 wherein the gene therapy is  
for the treatment of Parkinson's disease or nerve injury.

47. Use of a packaging-defective SIV provirus infected cell line in a method of introducing a heterologous nucleic acid sequence into a mammalian cell, wherein said heterologous gene sequence is comprised in an HIV-2 vector which further comprises an HIV-2 packaging signal.

48. Use according to claim 47 wherein the mammalian cell is a human or non-human primate cell.

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49. A method of delivering a therapeutic or antigenic protein or peptide to an individual comprising;

administering to the individual an effective amount of a virus according to claim 33 or 34, a vector system according to claim 38 or 39, a host cell according to any one of claims 35 to 37, or a pharmaceutical composition of claim 42.

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50. A method according to claim 49 wherein the individual is a human or non-human primate.

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51. A method of transfecting a cell with a heterologous nucleic acid sequence comprising;

producing a virus by a process according to according to any one of claims 1 to 28, and;

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contacting the virus with a target cell.

52. A method according to claim 51 wherein the target cell is a human or non-human primate cell.

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53. A method according to claim 51 or claim 52 wherein the cell is a CNS cell.

54. A method according to claim 53 wherein the cell is a glial cell, astrocyte, or neural stem cell.

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55. A method of determining the biosafety of an agent comprising;

administering to a non-human primate an effective amount of  
an agent selected from the group consisting of: a virus according  
to claim 33 or 34, a vector system according to claim 38 or 39 or  
a host cell according to any one of claims 35 to 37, or a  
5 pharamaceutical composition of claim 42,  
and determining the effect of said administration on the  
primate.

56. A method according to claim 55 wherein the non-human primate  
10 is a macaque or baboon.